

**IFWO** 

**RAW SEQUENCE LISTING**PATENT APPLICATION: **US/10/762,040**DATE: 08/30/2004

TIME: 13:07:00

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3 <110> APPLICANT: YON, Jeff
 4
         TICKLE, Ian
 5
         SHARFF, Andrew
         CLEASBY, Anne
 6
 7
         BRUINZEEL, Wouter David
 8
         MASURE, Stefan Leo Jozef
10 <120> TITLE OF INVENTION: Novel BACE Proteins, Nucleic Acid Molecules Therefor, Novel
         Crystal Structure of Novel BACE Proteins, and Methods for Making
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         and Using
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14 <130> FILE REFERENCE: 43962-010910
16 <140> CURRENT APPLICATION NUMBER: 10/762,040
17 <141> CURRENT FILING DATE: 2004-01-21
19 <150> PRIOR APPLICATION NUMBER: PCT/GB02/03461
20 <151> PRIOR FILING DATE: 2002-07-26
22 <150> PRIOR APPLICATION NUMBER: 60/308,366
23 <151> PRIOR FILING DATE: 2001-07-26
25 <160> NUMBER OF SEQ ID NOS: 72
27 <170> SOFTWARE: PatentIn version 3.2
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49 cgagcccaga gggcccgaag gccggggccc accatggccc aagccctgcc ctggctcctg
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51 ctgtggatgg gcgcgggagt gctgcctgcc cacggcaccc agcacggcat ccggctgccc
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|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|
| 77 aatggacagg atctgaaaat ggactgcaag gagtacaact atgacaagag cattgtggac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1320                                                                                                                          |
| 79 agtggcacca ccaaccttcg tttgcccaag aaagtgtttg aagctgcagt caaatccatc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1380                                                                                                                          |
| 81 aaggcageet eetecaegga gaagtteeet gatggtttet ggetaggaga geagetggtg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1440                                                                                                                          |
| 83 tgctggcaag caggcaccac cccttggaac attttcccag tcatctcact ctacctaatg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1500                                                                                                                          |
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| 87 gtggaagatg tggccacgtc ccaagacgac tgttacaagt ttgccatctc acagtcatcc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1620                                                                                                                          |
| 89 acgggcactg ttatgggagc tgttatcatg gagggcttct acgttgtctt tgatcgggcc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1680                                                                                                                          |
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| 93 geggtggaag geeettttgt cacettggae atggaagaet gtggetacaa cattecacag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1800                                                                                                                          |
| 95 acagatgagt caacceteat gaccatagee tatgteatgg etgecatetg egecetette                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1860                                                                                                                          |
| 97 atgctgccac tctgcctcat ggtgtgtcag tggcgctgcc tccgctgcct gcgccagcag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1920                                                                                                                          |
| 99 catgatgact ttgctgatga catctccctg ctgaagtgag gaggcccatg ggcagaagat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1980                                                                                                                          |
| 101 agagattccc ctggaccaca cctccgtggt tcactttggt cacaagtagg agacacagat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 2040                                                                                                                          |
| 103 ggcacctgtg gccagagcac ctcaggaccc tccccaccca ccaaatgcct ctgccttgat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 2100                                                                                                                          |
| 105 ggagaaggaa aaggctggca aggtgggttc cagggactgt acctgtagga aacagaaaag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 2160                                                                                                                          |
| 107 agaagaaaga agcactctgc tggcgggaat actcttggtc acctcaaatt taagtcggga                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 2220                                                                                                                          |
| 109 aattetgetg ettgaaactt cageeetgaa eetttgteea eeatteettt aaatteteea                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 2280                                                                                                                          |
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| 115 aagtcagtag gagaggatgc acagtttgct atttgcttta gagacaggga ctgtataaac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 2460                                                                                                                          |
| 117 aageetaaca ttggtgeaaa gattgeetet tgaattaaaa aaaaaaacta gaaaaaaaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 2520                                                                                                                          |
| 119 aaaaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 2526                                                                                                                          |
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| 124 <212> TYPE: DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                               |
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|     | cgctgcctcc  |             |             |            |             |            | 1500 |
|     | aagtgaggag  |             |             |            |             |            | 1560 |
|     | ctttggtcac  |             |             |            |             |            | 1620 |
|     | ccacccacca  |             |             |            |             |            | 1680 |
| 184 | ggactgtacc  | tataggaaac  | agaaaagaga  | agaaagaagc | actictected | caggaatact | 1740 |
|     | cttggtcacc  |             |             |            |             |            | 1800 |
| 188 | ttgtccacca  | ttcctttaaa  | ttctccaacc  | caaagtattc | ttcttttctt  | agtttcagaa | 1860 |
| 190 | gtactggcat  | cacacgcagg  | ttaccttggc  | atatateeet | ataataccct  | agceceagaa | 1920 |
| 192 | agaccaagct  | tatttcccta  | ctaaccaaaa  | tcagtaggag | aggatgcaca  | atttactatt | 1980 |
| 194 | tgctttagag  | acagggactg  | tataaacaag  | cctaacatto | gtgcaaagat  | tacatattaa | 2040 |
|     | attaaaaaaa  |             | cacaaaaaaaa | cocaacaccg | gegeddagae  | egectetiga | 2054 |
|     | <210> SEQ   |             |             |            | •           |            | 2034 |
|     | <211> LENG  |             |             |            |             |            |      |
|     | <212> TYPE  |             |             |            |             |            |      |
|     | <213> ORGA  |             | saniens     |            |             |            |      |
|     | <400> SEQUI |             | bapiens     |            |             |            |      |
|     | aaaaaaaaaa  |             |             |            |             |            | 16   |
|     | <210> SEQ   |             |             |            |             |            | 16   |
|     | <211> LENG' |             |             |            |             |            |      |
|     | <212> TYPE  |             |             |            |             |            |      |
|     | <213> ORGAI |             | saniens     |            |             |            |      |
|     | <400> SEQUI |             | Supremb     |            |             |            |      |
|     | atggcccaag  |             | actectacta  | tagatagaga | caaaaataat  | acatagagaa | 60   |
| 216 | ggcacccagc  | acggcat.ccg | actaccccta  | cacaacaaca | taggagagaga | cccctagaa  | 120  |
| 218 | ctgcggctgc  | cccadagaac  | cascasaaa   | cccaacaacc | ccaaccaaa   | aggaagetet | 180  |
| 220 | gtggagatgg  | tggacaacct  | aaaaaaaaaaa | tragaggage | actactacat  | gggcagcttt | 240  |
| 222 | gtgggcagcc  | ccccacagac  | gctcaacatc  | ctaataata  | canacaacaa  | taactttoca | 300  |
| 224 | gtgggtgctg  | cccccaccc   | cttcctgcat  | coctactacc | agaggagcag  | atacadaca  | 360  |
|     | taccgggacc  |             |             |            |             |            | 420  |
|     | ctgggcaccg  |             |             |            |             |            | 480  |
|     | gctgccatca  |             |             |            |             |            | 540  |
|     | gggctggcct  |             |             |            |             |            | 600  |
| 234 | ctggtaaagc  | agacccacgt  | tcccaacctc  | ttctccctcc | agetttataa  | tactacetta | 660  |
| 236 | ccctcaacc   | agtetgaagt  | actagactet  | atcagagaga | agettegegg  | tgaaggtata | 720  |
|     | gaccactcgc  |             |             |            |             |            | 780  |
|     | gaggtgatca  |             |             |            |             |            | 840  |
| 242 | tacaactatg  | acaagaggat  | tataaceat   | ggacaggacc | agattaattt  | aggaaagaaa | 900  |
| 244 | gtgtttgaag  | ctacaatcaa  | atccatcaac  | ggeaccacca | acceçegeee  | gttaggtgat |      |
| 246 | ggtttctggc  | taggagaga   | acteatetas  | tagazzagza | ccacggagaa  | ttäanaatt  | 960  |
| 248 | ttcccactca  | tataaatata  | getggtgtgt  | gagettagga | gcaccaccec  | aggataac   | 1020 |
| 250 | ttcccagtca  | aggantaggt  | aggagagata  | gaggitacca | accagiecti  | cegeateace | 1080 |
| 250 | atcetteege  | agcaacaccc  | geggeeageg  | gaagatgtgg | ceaegreeea  | agacgactgt | 1140 |
| 254 | tacaagtttg  | ttatatttaa  | tagagagaga  | ggcactgtta | cygyagetgt  | catcatggag | 1200 |
| 254 | ggcttctacg  | atgrattar   | anganan     | adacyaattg | geetigetgt  | cagegettge | 1260 |
|     | catgtgcacg  |             |             |            |             |            | 1320 |
| 250 | gaagactgtg  | geracaacat  | ccacagaca   | gatgagtcaa | ccctcatgac  | catagectat | 1380 |
| ∠0U | gtcatggctg  | ecatetgege  | celetteatg  | cigecaetet | gcctcatggt  | grgrcagtgg | 1440 |
|     |             |             |             |            |             |            |      |

## RAW SEQUENCE LISTING

DATE: 08/30/2004 TIME: 13:07:00

PATENT APPLICATION: US/10/762,040

Input Set : A:\US10-762040.txt
Output Set: N:\CRF4\08302004\J762040.raw

|     | cgctgcctcc gctgcctgcg ccagcagcat | gatgactttg | ctgatgacat | ctccctgctg | 1500 |
|-----|----------------------------------|------------|------------|------------|------|
|     | aagtga                           |            |            |            | 1506 |
|     | <210> SEQ ID NO: 5               |            |            |            |      |
|     | <211> LENGTH: 4                  |            |            |            |      |
|     | <212> TYPE: DNA                  |            |            | •          |      |
|     | <213> ORGANISM: Homo sapiens     |            |            |            |      |
|     | <400> SEQUENCE: 5                |            |            |            |      |
|     | atgc                             |            |            |            | 4    |
|     | <210> SEQ ID NO: 6               |            |            |            |      |
|     | <211> LENGTH: 6                  |            |            | •          |      |
|     | <212> TYPE: DNA                  |            |            |            |      |
|     | <213> ORGANISM: Homo sapiens     |            |            | •          |      |
|     | <400> SEQUENCE: 6                |            |            | •          |      |
|     | tactag                           |            |            |            | 6    |
| 285 | <210> SEQ ID NO: 7               |            |            | •          |      |
| 286 | <211> LENGTH: 5                  |            |            |            |      |
|     | <212> TYPE: DNA                  |            |            |            |      |
| 288 | <213> ORGANISM: Homo sapiens     |            |            |            |      |
| 290 | <400> SEQUENCE: 7                |            |            |            |      |
| 291 | taaat                            |            |            |            | 5    |
| 294 | <210> SEQ ID NO: 8               |            |            |            |      |
| 295 | <211> LENGTH: 8                  |            |            |            |      |
| 296 | <212> TYPE: DNA                  |            |            |            |      |
| 297 | <213> ORGANISM: Homo sapiens     |            |            |            |      |
| 299 | <400> SEQUENCE: 8                |            |            |            |      |
| 300 | cagtcaca                         |            |            |            | 8    |
|     | <210> SEQ ID NO: 9               |            |            |            |      |
|     | <211> LENGTH: 10                 |            |            |            |      |
| 305 | <212> TYPE: DNA                  |            |            |            |      |
|     | <213> ORGANISM: Homo sapiens     |            |            |            |      |
|     | <400> SEQUENCE: 9                |            |            |            |      |
|     | ccaaggcttc                       |            |            |            | 10   |
|     | <210> SEQ ID NO: 10              |            |            |            |      |
|     | <211> LENGTH: 9                  |            |            |            |      |
|     | <212> TYPE: DNA                  |            |            |            |      |
|     | <213> ORGANISM: Homo sapeins     |            |            |            |      |
|     | <400> SEQUENCE: 10               |            |            |            |      |
|     | aataaggaa                        |            |            |            | 9    |
|     | <210> SEQ ID NO: 11              |            |            |            | _    |
|     | <211> LENGTH: 5                  |            |            |            |      |
|     | <212> TYPE: DNA                  |            |            |            |      |
|     | <213> ORGANISM: Homo sapiens     |            |            |            |      |
|     | <400> SEQUENCE: 11               |            |            |            |      |
|     | cacac                            |            |            |            | 5    |
|     | <210> SEQ ID NO: 12              |            |            |            | 5    |
|     | <211> LENGTH: 4                  |            |            |            |      |
|     | <212> TYPE: DNA                  |            |            |            |      |
|     | <213> ORGANISM: Homo sapiens     |            |            |            |      |
|     | <400> SEQUENCE: 12               |            |            |            |      |
| ,,, | TOUR DEQUENCE. IZ                |            |            |            |      |

RAW SEQUENCE LISTING DATE: 08/30/2004 PATENT APPLICATION: US/10/762,040 TIME: 13:07:00

Input Set : A:\US10-762040.txt

| 336  | aagc                                |         |   |   | 4   |
|------|-------------------------------------|---------|---|---|-----|
| 339  | <210> SEQ ID NO: 13                 |         |   |   |     |
| 340  | <211> LENGTH: 17                    |         |   |   |     |
| 341  | <212> TYPE: DNA                     |         | · |   |     |
| 342  | <213> ORGANISM: Homo                | sapiens |   |   |     |
|      | <400> SEQUENCE: 13                  | _       |   |   |     |
|      | aagatggtaa gcgctat                  |         |   |   | 17  |
|      | <210> SEQ ID NO: 14                 |         |   |   |     |
|      | <211> LENGTH: 9                     |         |   |   |     |
| 350  | <212> TYPE: DNA                     |         |   |   |     |
| 351  | <213> ORGANISM: Homo                | sapiens |   |   |     |
|      | <400> SEQUENCE: 14                  |         |   |   |     |
|      | tgttttata                           |         |   |   | 9   |
|      | <210> SEQ ID NO: 15                 |         |   |   |     |
|      | <211> LENGTH: 13                    |         |   |   |     |
|      | <212> TYPE: DNA                     |         |   |   |     |
|      | <213> ORGANISM: Homo                | sapiens |   |   |     |
|      | <400> SEQUENCE: 15                  | Dapid   |   |   |     |
|      | tgcttttggc agc                      |         |   |   | 13  |
|      | <210> SEQ ID NO: 16                 |         |   |   | 1.7 |
|      | <211> LENGTH: 5                     |         |   | - |     |
|      | <212> TYPE: DNA                     |         |   |   |     |
|      | <213> ORGANISM: Homo                | saniens |   |   |     |
|      | <400> SEQUENCE: 16                  | bapieno |   |   |     |
|      | agetq                               |         |   |   | 5   |
|      | <210> SEQ ID NO: 17                 |         |   |   | ,   |
|      | <211> LENGTH: 4                     |         |   |   |     |
|      | <212> TYPE: DNA                     |         |   |   |     |
|      | <213> ORGANISM: Homo                | saniens |   |   |     |
|      | <400> SEQUENCE: 17                  | bapieno | • |   |     |
|      | ctca                                |         |   |   | 4   |
|      | <210> SEQ ID NO: 18                 |         |   |   |     |
|      | <211> LENGTH: 5                     |         |   |   |     |
|      | <212> TYPE: DNA                     |         |   |   |     |
|      | <213> ORGANISM: Homo                | saniens |   |   |     |
|      | <400> SEQUENCE: 18                  | Dapiens |   |   |     |
|      | ttctq                               |         |   |   | 5   |
|      | <210> SEQ ID NO: 19                 |         |   |   | ,   |
|      | <211> LENGTH: 13                    |         |   |   |     |
|      | <212> TYPE: DNA                     |         |   |   |     |
|      | <213> ORGANISM: Homo                | saniens |   |   |     |
|      | <400> SEQUENCE: 19                  | Bapiens |   |   |     |
|      | cetttgetge gga                      |         |   |   | 13  |
|      | <210> SEQ ID NO: 20                 |         |   |   | 13  |
|      | <211> SEQ 1D NO: 20 <211> LENGTH: 8 |         |   |   |     |
|      | <211> LENGTH: 8 <212> TYPE: DNA     |         |   |   |     |
|      | <213> ORGANISM: Homo                | canienc |   |   |     |
|      | <400> SEQUENCE: 20                  | pahreng |   |   |     |
|      | tccgaatt                            |         |   |   | . 8 |
| -100 | cccyaacc                            |         |   |   | 0   |
|      |                                     |         |   |   |     |

RAW SEQUENCE LISTING ERROR SUMMARY

DATE: 08/30/2004

PATENT APPLICATION: US/10/762,040

TIME: 13:07:01

Input Set : A:\US10-762040.txt

Output Set: N:\CRF4\08302004\J762040.raw

## Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:46; N Pos. 3,4,11,26,28,45,55,57,60,64,68,70,73,77

Seq#:47; N Pos. 6,7

VERIFICATION SUMMARY

DATE: 08/30/2004

PATENT APPLICATION: US/10/762,040

TIME: 13:07:01

Input Set : A:\US10-762040.txt

Output Set: N:\CRF4\08302004\J762040.raw

J:1208 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:46 after pos.:0 L:1210 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:46 after pos.:60 L:1225 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:47 after pos.:0